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# Effectiveness of Web- and Mobile-Based Treatment of Subthreshold Depression With Adherence-Focused Guidance: A Single-Blind Randomized Controlled Trial

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**Evidence for the impact of psychological Interventions for subthreshold depression (sD) is conflicting. Moreover, human resources to deliver such treatments are limited. This study aimed to evaluate the effectiveness of a web-based intervention with adherence-focused guidance in the treatment of sD. Participants with sD (CES-D≥ 16, no Major Depressive Disorder according to DSM-IV criteria, $N = 204$) recruited via**

**a large health insurance were randomly allocated to a web-based mobile-supported cognitive-behavioral intervention or to a waitlist control condition with unrestricted access to usual care. The primary outcome was the reduction in depressive symptom severity as measured by blind diagnostic raters using the Quick Inventory of Depressive Symptomatology (QIDS) at posttreatment. There was a statistically significant between-group difference in QIDS scores at posttreatment in favor of the intervention group, $F(1, 201) = 11.31$, $p = .001$, corresponding to a medium effect size of $d = 0.37$ (95% CI 0.09–0.64) and a NNT of 7 (95%–CI 3.7–41.2). Significant effects in favour of the intervention group were also found for secondary outcomes such as quality of life, anxiety, and insomnia severity. Web-based self-help interventions with adherence-focused guidance could be an acceptable and effective approach to reduce a range of negative consequences associated with subclinical depression.**

*Keywords:* subthreshold depression; minor depression; web-based intervention; clinician-rated

Subthreshold depression can be defined dimensionally (i.e., scoring above a cutoff level on a validated self-rated depression screening measure while the criteria of a full-blown depressive disorder are not yet met according to a diagnostic interview) or categorically (i.e., fewer than five symptoms of depression according to the DSM-IV, for instance, are present) (Baumeister, 2012; Cuijpers, Koole, et al., 2014). Subthreshold depression is a highly prevalent condition (Cuijpers, de Graaf, & van Dorsselaer, 2004) related to increased mortality (Cuijpers, Vogelzangs, et al., 2013), poorer quality of life (Rucci et al., 2003), increased health care service utilization (Goldney, Fisher, Dal Grande, & Taylor, 2004), and vast societal costs (Cuijpers et al., 2007). From a clinical perspective, subthreshold depression is not only important because it can be a disabling condition, but also due to the associated risk of developing major depression. Subthreshold depression can be regarded as part of the prodromal phase of major depression (Eaton, Badawi, & Melton, 1995). Almost all individuals who have developed a major depression are assumed to have initially passed through a period of subthreshold depression (Frank et al., 1991), underscoring the importance of preventive interventions aimed at the treatment of subthreshold depression and the prevention of major depression.

In contrast to major depressive disorder, however, there are only a few studies on the effectiveness of psychological treatments for subthreshold depression. A recent meta-analysis showed small-to-moderate effect sizes of psychological interventions on depressive symptom severity at posttreatment compared to usual care (Cuijpers, Koole, et al., 2014). Notwithstanding, the four studies using clinician-rated outcomes did not indicate significant positive results. As effects of psychological interventions for the treatment of subthreshold depression are expected to be small to moderate in size only, cost-effective delivery modes are particularly needed. The Internet offers an opportunity to deliver psychological interventions to a large audience at lower costs than face-to-face interventions, depending on the level of human support involved.

The efficacy of web-based interventions for major depression is very well researched. Treatment effects for web-based cognitive behavioral therapy for depression or depressive symptoms are large in size (SMD 0.94, 95% CI 0.77-1.11; 20 RCTs; Ebert et al., 2015; Hedman, Ljotsson, & Lindefors, 2012). Effect sizes at posttreatment range from $d = 1.35$ for guided interventions, $d = .95$ for administrative-supported interventions, to $d = .78$ for unguided interventions (Richards & Richardson, 2012). As face-to-face psychological interventions show smaller effects in subthreshold depression compared to major depression (Cuijpers, Koole, et al., 2014), it is important to assess the usefulness of web-based interventions in subthreshold depression. However, the evidence base for the effectiveness of web-based interventions in subthreshold depression is still limited. Three randomized controlled trials have

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MB and DE obtained funding for this study. All authors contributed to the conception and design of the overall study, which was led by DE and CB. DE and CB analysed and interpreted the clinical data. DE and CB drafted the manuscript. All authors revised the article critically for important intellectual content and gave final approval of the version to be published.

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been conducted that have tested the efficacy of web-based interventions in the treatment of subthreshold depression (Buntrock et al., 2015; Buntrock et al., 2016; Imamura et al., 2014; Spek et al., 2007). Buntrock and colleagues (2015, 2016) showed that a web-based intervention with intensive guidance (up to 3 hours per participant) was effective in treating subthreshold depression and in preventing the onset of major depressive disorder. However, the amount of intensive guidance clearly places constraints for scaling up this intervention. Therefore, we evaluated the same web-based intervention with minimal guidance (i.e., adherence-focused guidance), as such an intervention may cost less and will be associated with fewer constraints for scaling up.

The adherence-focused guidance concept was in line with the supportive accountability model (Mohr, Cuijpers, & Lehman, 2011). This model assumes that adherence to a web-based intervention (and therefore the effectiveness) could be enhanced via human support through accountability to an e-coach who is seen as legitimate, trustworthy, benevolent, and having expertise. The e-coach guidance consists of two elements: (a) adherence monitoring and (b) feedback on demand. Both personal and automatic reminders have shown to improve adherence to self-guided health promotion and behavior change interventions (Titov et al., 2013). However, it is assumed that personal as opposed to automatic reminders from an e-coach are perceived as more benevolent and are, therefore, more effective. Feedback on demand provides participants with the opportunity to contact an e-coach via the internal messaging function on the platform and to receive individual support/feedback whenever desired. Feedback is not assumed to have a direct influence on the effectiveness of the intervention, but expected to create a sense that the e-coach is legitimate and has the participant's best interest at heart. Individuals are assumed to respond more positively to adherence demands from an e-coach who is perceived as legitimate (Ebert et al., 2016; Tyler, 1997; Zarski et al., 2016). This guidance format is expected to offer the positive effects of regular guidance while keeping the time spent per participant to a minimum, thus producing a more economic version of the guided web-based intervention.

This study aimed to evaluate the effectiveness of a web-based intervention with adherence focused guidance in the treatment of subthreshold depression. We hypothesized that the effectiveness of the web-based intervention with clinician-rated depressive symptom severity at posttreatment as its main outcome was superior to a waitlist control group with unrestricted access to usual care.

## Methods

### DESIGN

A two-armed, pragmatic single-blind randomized controlled clinical trial was conducted to compare an adherence-focused guided web-based intervention (GET.ON Mood Enhancer) with a waitlist control condition with unrestricted access to care-as-usual. Assessments took place at baseline (diagnostic interviews, online questionnaires), at posttreatment (7 weeks; diagnostic interviews, online questionnaires), and at 3-month follow-up (online questionnaires only; see Figure 1 for a detailed overview of assessments). The study was approved by the Medical Ethics Committee of the University of Lueneburg (reference number Ebert201404_Depr) and registered under DRKS00005973 in the German clinical trial registry.

### STUDY POPULATION AND RECRUITMENT

Study participants were recruited from the general population via a large German health insurance company (BARMER GEK), through newspaper articles, on-air media, and related websites. Referral by a GP was not required. The present trial is a follow-up study of a prevention trial that assessed the (cost-) effectiveness of the web-based intervention with intensive guidance on the onset of major depressive disorder. After the enrollment of the first study was completed, there were still more than 700 applicants on a waitlist for study participation. Applicants self-identifying with a diminished mood who (a) screened positive for subthreshold depressive symptoms (Centre for Epidemiological Studies Depression Scale [CES-D] $\geq$ 16; Lewinsohn, 1974), (b) were aged 18 and above, (c) had Internet access, (d) were not currently receiving or (e) on a waiting list for psychotherapy for any kind of mental health problem, (f) had had no psychotherapy for any kind of mental health disorder in the past 6 months, and (g) had no notable suicidal risk (BDI item 9 > 1) were scheduled for a semistructured clinical interview (SCID) conducted by telephone by trainees in psychotherapy to assess final eligibility. Those meeting DSM-IV criteria for (a) a major depressive episode, (b) bipolar disorder, or (c) psychotic disorder, and (d) having a history of a major depressive disorder in the past 6 months according to Kupfer's model (Kupfer, 1991) were excluded. According to Kupfer's model, a patient is considered to be recovered when he or she stays in remission for a minimum of 6 months. As we conducted a pragmatic trial, the use of antidepressant medication was allowed as part of care-as-usual. However, participants needed to be on a stable dose for at least 4 weeks to be able to enter the study.

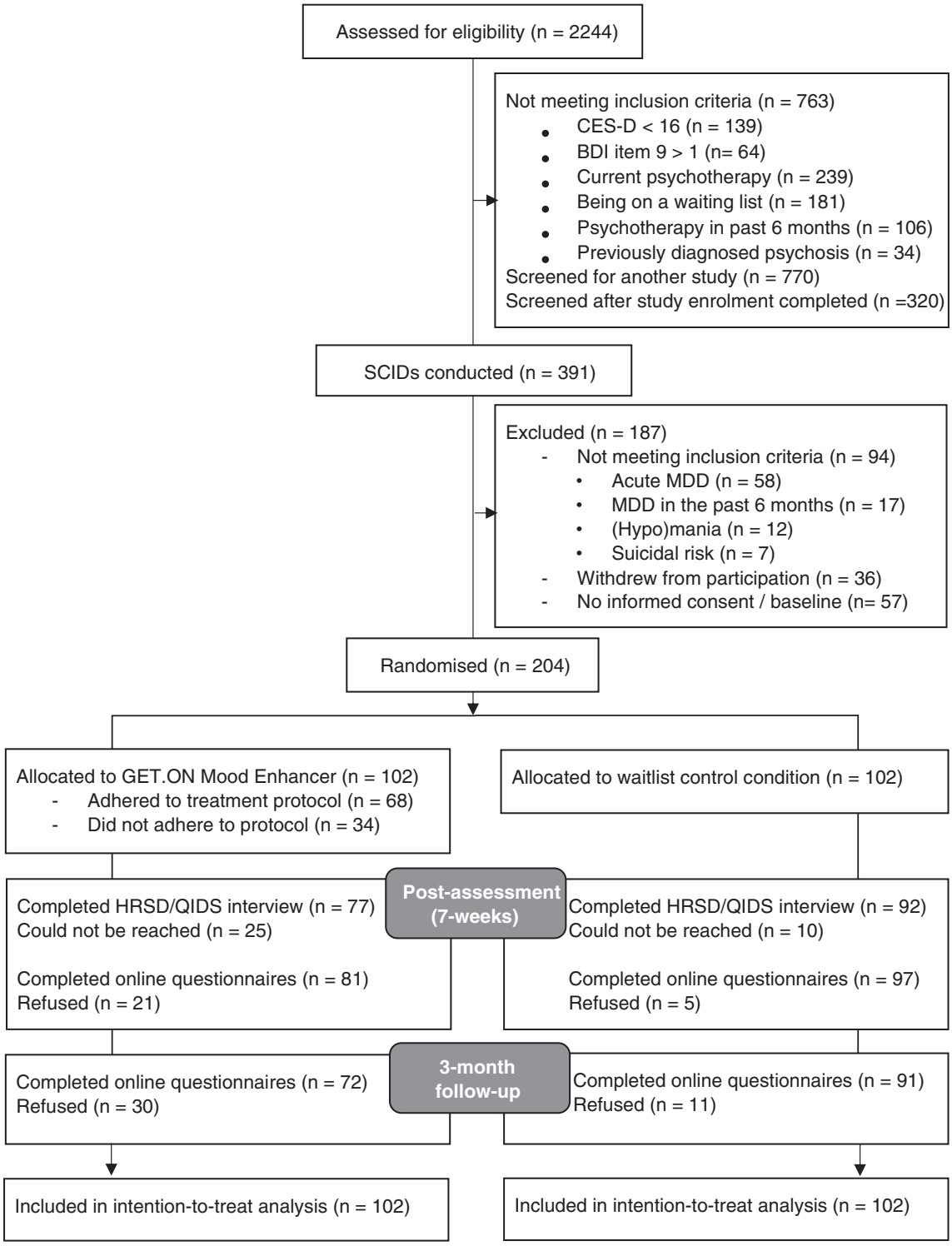


FIGURE 1 Study flow chart.

### RANDOMIZATION AND MASKING

Participants passing all inclusion and exclusion criteria who completed the baseline assessment and returned their informed consent form were randomly allocated to study conditions. Randomization took place at individual level and was conducted centrally by an independent researcher not otherwise involved in the study using an automated computer-generated

random numbers table. Block randomization of size twelve was used to ensure equity of sample sizes across study conditions. As usual for psychological intervention trials, study participants knew their allocation. The research staff conducting the observer-based rating of depressive symptom severity were blind to treatment allocation. Steps to ensure blindness included the following: (a) an explanation to participants as to why it is important not to inform the interviewer about the condition to which they were assigned; (b) a written reminder in the interview manual for the interviewer to ask participants not to disclose their randomization status; (c) verbal reminders to participants before the interview; and (d) a documentation after the assessment of whether or not the interviewer was still blind to the treatment condition.

## INTERVENTIONS

All study participants had unrestricted access to routine care (i.e., visits to the GP). According to the German S3-Guideline/National Disease Management Guideline Unipolar Depression, more intensive psychological interventions (i.e., cognitive behavioral therapy) should only be offered if depressive symptoms intensify (i.e., diagnosed major depressive disorder) (Bundesärztekammer, Bundesvereinigung, & Fachgesellschaften, 2011). Following the S3-Guideline, usual care is then subsequently stepped up to more intensive interventions (i.e., psychotherapy or prescription of antidepressant medication). In this pragmatic trial, usual care was not protocolized. Participants in the control condition received access to the web-based intervention 3 months after randomization.

### *Web-Based Intervention*

The web-based intervention consists of six 30-minute interactive sessions. However, the duration of sessions might vary across users. Four weeks after finishing the intervention, participants are offered an optional booster session. The aim of this session is to evaluate progress and to strengthen skills acquired during the intervention. Intervention sessions include text, exercises, testimonials, and audio and video clips. Audio sequences introduce relaxation exercises, whereas video clips explain theoretical frameworks in a user-friendly way. Based on studies suggesting that a higher treatment session frequency might be associated with a better outcome (Cuijpers, Huibers, Ebert, Koole, & Andersson, 2013), participants were advised to complete two sessions a week, if possible, but a minimum of at least one. Intervention usage was monitored by logfile analysis. The intervention is based on behavior therapy (BT) and problem-solving therapy (PST), the content of which has been described in detail elsewhere by Buntrock et al. (Buntrock et al., 2015; Buntrock et al., 2016). A detailed description of the intervention can be found in the supplemental online material. During the study, a strong emphasis was placed on homework assignments meant to help the integration of acquired coping skills into daily life. As an optional component, participants could choose to receive a set of roughly 42 standardized text-messages supporting them in this integration.

During the intervention, participants were supported by an e-coach applying an adherence-focused guidance concept. Trained and supervised graduate students as well as health care professionals served as e-coaches and provided guidance. Adherence monitoring included checking whether participants completed intervention sessions and, if not, reminding them to do so. The e-coach sent reminders if participants did not complete a session within 7 days. Feedback was provided only upon request of the intervention users as part of a feedback on demand approach. Within 48 hours, the participants received personalized written feedback. The feedback provided by the e-coaches focused on supporting participants to work through the exercises and no therapeutic advice was given.

## OUTCOMES

Self-report measures were collected at baseline, posttreatment, and 3-month follow-up. We used a secured online-based assessment system (AES, 256-bit encrypted). The diagnostic interviews at baseline and posttreatment were conducted by telephone.

### *Primary Outcome*

*Depressive symptom severity.* The primary outcome was depressive symptom severity as measured by the 16-item Quick Inventory of Depressive Symptomatology–Clinician-Rating (QIDS-CR16). The QIDS-CR16 evaluates the nine depression criterion symptom domains, as stated in the DSM-IV, during the prior 7 days, providing a nuanced understanding of the symptom severity. Each item is scored on a scale from 0 to 3, with higher scores indicating higher symptom severity. The QIDS has shown good psychometric properties, such as strong internal consistency ($\alpha = 0.85$), concurrent validity, and sensitivity to symptom change in patients with major depression (Trivedi et al., 2004). Cutoff points of 6, 11, 16, and 21 represent the thresholds for mild, moderate, severe, and very severe depressive symptom severity, respectively. Interrater reliability was assessed by rating audiotaped diagnostic interviews by an independent experienced diagnostic rater. Interrater reliability based on data of 10% of participants was 0.97.

*Secondary Outcomes*

*Mental health*. Among the secondary outcomes concerning mental health, the following outcomes were measured using the specified scales: *depression*, using the Hamilton Rating Scale for Depression ([HRSD-24]; interrater reliability 0.94). The HRSD is a widely used clinician-rated scale for measuring depression with high internal consistency ($\alpha = .88$) and sensitivity to change over time and treatment. The cutoff points of 10, 19, 27, and 35 indicate the thresholds for mild, moderate, severe, and very severe depressive symptom severity, respectively (Rush et al., 2003). Self-reported depressive symptomatology was measured with the Center for Epidemiological Studies Depression Scale (CES-D; Radloff, 1977; 20 items, range 0–60, $\alpha = .78$). Using the HRSD and the CES-D allowed for a more detailed comparison with previous research. *Anxiety*, using the anxiety subscale of the Hospital Anxiety and Depression Scale (HADS-A; Zigmond & Snaith, 1983; 7 items, range 0–21, $\alpha = .67$); *worrying*, using the ultra-brief version of the Penn State Worry Questionnaire (PSWQ; Berle et al., 2011; 3 items, range 0–18, $\alpha = .84$); *insomnia severity*, using the Insomnia Severity Index (ISI; Bastien, Vallieres, & Morin, 2001; 7 items, range 0–28, $\alpha = .86$); and *alcohol use disorders*, using the Alcohol Use Disorders Identification Test (AUDIT; Saunders, Aasland, Babor, de la Fuente, & Grant, 1993; 10 items, range 0–40, $\alpha = .80$).

*Treatment Mechanism Measures*

Behavioral activation, using the Behavioural Activation for Depression Scale–Short Form (BADS-SF; Manos, Kanter, & Luo, 2011; 9 items, range 0–56, $\alpha = .68$); problem-solving skills in terms of positive problem orientation, using the positive problem orientation subscale of the Social Problem-Solving Inventory-Revised (SPSI-R; D'Zurilla, Nezu, & Maydeu-Olivares, 2002; 5 items, range 0–20, $\alpha = .77$) and negative problem orientation, using the negative problem orientation subscale of the SPSI-R (5 items, range 0–20, $\alpha = .85$); and mastery, using the Pearlin Mastery Scale (PSMS; Pearlin & Schooler, 1978; 7 items, range 0–21, $\alpha = .72$) were assessed as measures of treatment mechanism.

## SAMPLE SIZE

Based on a meta-analysis of psychological treatments for subthreshold depression (Cuijpers, Koole, et al., 2014), this trial was powered to detect a mean difference of $d = 0.35$ in the primary outcome between the groups at posttreatment, with an $\alpha$ of 0.05 and a power of 80% in a one-tailed test. A one-tailed test was applied based on the unidirectional hypothesis that the intervention group is superior compared to the control group. This assumption is supported by the first trial on this intervention (Buntrock et al., 2015; Buntrock et al., 2016). Based on the power calculation, we needed to include 204 participants.

## DATA ANALYSES

All analyses are reported according to the CONSORT statement (Schulz, Altman, & Moher, 2010). Following the intention-to-treat principle, all analyses were based on the imputed dataset. All analyses were performed with IBM SPSS v. 22. All reported $p$-values are one-sided with a significance level of 0.05. Missing data were imputed using a Markov Chain Monte Carlo multivariate imputation algorithm (missing data module in SPSS 22) with 10 estimations per missing value. In addition, per protocol analyses were conducted based on the sample of participants who adequately adhered to the intervention protocol. Participants were classified as intervention completers if they adhered to at least 80% of the intervention (5 out of 6 sessions). We also performed analyses to assess whether intervention completers differed from noncompleters in terms of demographic characteristics or baseline depressive symptom severity. We used analysis of covariance (ANCOVA) to compare outcomes between groups at posttreatment and at 3-month follow-up adjusting for baseline scores. Because income levels were unequally distributed between study conditions, income was also included as covariate into the model (post hoc). As income was not a predictor of the outcome, it was excluded from the final model. Results were reported as mean within- and between-group differences and as Cohen's $d$ effect sizes (and their 95% CIs according to Hedges and Olkin, 1985) controlling for baseline data (i.e., calculating change scores divided by the pooled standard deviation of change scores). Improvements on the primary outcome at individual level were examined by assessing the number of participants who displayed a treatment response and symptom-free status. Response represented significant symptomatic improvement, whereas symptom-free status represented improvement to the point of being asymptomatic within a normal range. In studies of acute treatment for depression, response is most consistently defined as at least a 50% reduction in the symptom score from baseline on a standardized rating scale (i.e., QIDS and HRSD) (Israel, 2006). However, in studies of the treatment of subclinical forms of depression, the reliable change index (RCI) as proposed by Jacobson and Truax (1991) is often used to define treatment response (Buntrock et al., 2015; Haringsma, Engels, Cuijpers, & Spinhoven, 2006; Spek et al., 2007; Vazquez et al., 2012). Thus, to use similar criteria across studies and to facilitate comparisons, we applied the RCI in addition to the 50%

reduction in symptom score from baseline. Participants were defined as reliably improved if their QIDS (HRSD) score declined from baseline to posttreatment with more than 1.96 standard units, while also taking into account the reliability of the measurement instruments to compensate for measurement error. Participants met criteria for reliable change when they had improved at least 3.60 points on the QIDS and 4.47 points on the HRSD, respectively. Symptom-free status was defined a priori as a nonpathological score of < 6 on the QIDS and of < 10 on the HRSD24 (Rush et al., 2003; Trivedi et al., 2004). Patients scoring in the normal range of the QIDS and HRSD at baseline were excluded from the analyses. Numbers needed-to-treat (NNT; with 95% CI) to achieve one additional response and symptom-free status, respectively, were calculated as the inverse of the risk difference (Kraemer & Kupfer, 2006). We performed sensitivity analyses to test whether treatment duration and receiving treatment during the follow-up period were predictors of the outcome. In addition, primary intervention effects were assessed on the study completers' sample.

## RESULTS

### *Participants*

Participant characteristics at baseline are shown in Table 1. In brief, participants were predominantly female (80.4%), of an average age of 44 years (*SD* 11.7), had an above-average level of education (A-level or higher: 81.9%), and were employed (86.8%). Four out of 10 participants have received psychotherapy at some point in their lives ($n$ = 82; 40.2%). There were no clinically important differences between treatment conditions in terms of any baseline characteristic indicating that randomization was successful. Figure 1 illustrates the enrollment and flow of participants through the study. A

Table 1
Baseline Characteristics According to Study Group (Mean and Standard Deviation or Number and Percentage)

| Characteristic | Intervention group (n=102) | Control group (n=102) | Total sample (N=204) |
|---|---|---|---|
| QIDS sum score | 8.17 (3.62) | 8.11 (3.90) | 8.14 (3.75) |
| HRSD sum score | 13.72 (6.20) | 14.63 (6.81) | 14.17 (6.52) |
| CES-D sum score | 26.67 (6.50) | 27.73 (7.50) | 27.20 (7.02) |
| Use of antidepressants | 7 (6.9%) | 6 (5.9%) | 13 (6.4%) |
| Age | 44.66 (11.65) | 43.75 (11.84) | 44.20 (11.73) |
| Gender | | | |
| Male | 20 (19.6%) | 20 (19.6%) | 40 (19.6%) |
| Female | 82 (80.4%) | 82 (80.4%) | 164 (80.4%) |
| Relationship | | | |
| Single | 27 (26.5%) | 28 (27.5%) | 55 (27.0%) |
| Married or cohabiting | 65 (63.7%) | 53 (52.0%) | 118 (57.8%) |
| Divorced or separated | 9 (8.8% | 20 (19.6%) | 29 (14.2%) |
| Widowed | 1 (1.0%) | 1 (1.0%) | 2 (1.0%) |
| Ethnicity | | | |
| Caucasian | 79 (77.5%) | 81 (79.4%) | 160 (78.4%) |
| Not reported | 23 (22.5%) | 21 (20.6%) | 44 (21.6%) |
| Level of education | | | |
| Low (primary) | 2 (2.0%) | 3 (2.9%) | 5 (2.5%) |
| Middle (secondary) | 16 (15.7%) | 16 (15.7%) | 32 (15.7%) |
| High (A-level or higher) | 84 (82.4%) | 83 (81.4%) | 167 (81.9%) |
| Employment status | | | |
| Employed | 90 (88.3%) | 87 (85.3%) | 177 (86.8%) |
| Unemployed or seeking work | 2 (2.0%) | 4 (3.9%) | 6 (2.9%) |
| On sick leave | 0 (0%) | 2 (2.0%) | 2 (1.0%) |
| Non-working | 10 (9.8%) | 9 (8.8%) | 19 (9.3%) |
| Income in Euro [a] | | | |
| Low (< 10.000) | 9 (8.8%) | 25 (24.5%) | 34 (16.7%) |
| Middle (10 - 60.000) | 70 (68.6%) | 59 (57.8%) | 129 (63.2%) |
| High (> 60.000) | 14 (13.7%) | 10 (9.8%) | 24 (11.8%) |
| Not reported | 9 (8.8%) | 8 (7.8%) | 17 (8.3%) |

*Note.* QIDS = Quick Inventory of Depressive Symptomatology. HRSD = Hamilton Rating Scale for Depression. CES-D = Center for Epidemiological Studies Depression Scale.
[a] Gross annual income.

total of 204 participants were included in the study. Dropout rates differed between study groups at posttreatment and 3-month follow-up. As can be seen, dropout was higher in the intervention group (HRSD/QIDS interview posttreatment: $\chi^2(1) = 7.76$, $p = .005$; online questionnaires posttreatment: $\chi^2(1) = 11.28$, $p = .001$; online questionnaires 3-month follow-up: $\chi^2(1) = 11.02$, $p = .001$). Study dropout was not associated with baseline depressive symptom severity (p = .92) or any socio-demographic factor (lowest *p*-value = .11 for income). However, study dropout was associated with being in the intervention group, $\chi^2(1, n = 204) = 12.57, p < .001$. Eleven participants (5.4%) informed interviewers about their randomization status during the HRSD/QIDS follow-up interview (intervention group: 8/102, 7.8%; control group: 3/102, 2.9%).

*Intervention Usage, Reminders, and Content Feedbacks*

The average treatment duration was 7 weeks (*SD* = 3.17) and participants completed on average 5 sessions (*SD* = 2.25). Out of the 102 participants who were initially assigned to the intervention, 68 (66.7%) were intervention completers. Of those, 63 (92.6%) adhered to all six sessions. The booster session was completed by 40 (39.2%) participants. Of the 34 participants (33.3%) not completing 80% of the intervention, 6 participants never started the intervention (5.9%). Intervention completers did not significantly differ from noncompleters with regard to any baseline characteristics (lowest *p*-value = .20 for depressive symptom severity based on the QIDS).

The e-coaches spent on average 30 minutes on each participant. In total, the e-coaches sent 301 reminders corresponding to a mean of 3.07 reminders per participant (range: 0–9, *SD* = 2.08). Interestingly, only a few participants (*n* = 6, 5.88%) requested feedback, resulting in 15 content feedbacks for the entire sample. This corresponds to an average of 0.15 feedback demands per participant (range: 0–5, *SD* = 0.71). Thus, most time spent per participant was related to checking adherence and providing reminders.

*Primary Intervention Outcome*

Table 2 shows means, standard deviations, and between-group effect sizes of the clinical outcomes based on the intention-to-treat sample. Both study groups displayed statistically significant reductions in depressive symptom severity as indicated by changes in baseline to posttreatment scores in the QIDS (Table 2). Based on the QIDS, corresponding within-group Cohen's *d* effect sizes were 0.95 (95% CI 0.66–1.24) for the intervention group and 0.52 (95% CI 0.24–0.80) for the control group, respectively. As hypothesized, there was a statistically significant between-group difference in QIDS scores at posttreatment in favor of the intervention group, $F(1, 201) = 11.31$, $p = .001$. This difference in QIDS scores corresponded to a small to medium between-group effect size of 0.37 (95% CI 0.09–0.64). Per protocol analyses showed that intervention completers did not differ significantly from noncompleters regarding QIDS scores at posttreatment, $F(1, 99) = .001$, $p = .99$.

*Secondary Outcomes*

We found a statistically significant between-group difference in HRSD scores at posttreatment in favor of the intervention group (HRSD: $F[1, 201] = 7.36$, $p = .007$). This difference in HRSD scores corresponded to a small between-group effect size of 0.23 (95% CI -0.05–0.50). There were significant between-group differences for secondary outcomes favoring the intervention group except for mastery (Pearlin Mastery Scale; $p = 0.18$), negative problem-orientation (subscale of the SPSI; $p = 0.34$), and alcohol use (AUDIT; $p = 0.10$). The effect sizes of the secondary outcomes ranged from $d = 0.41$ (95% CI 0.13–0.68) (HADS-A) to $d = 0.71$ (95% CI 0.43–0.99) (CES-D) (Table 2).

*Response and Symptom-Free Status*

Based on the QIDS and HRSD, a score reduction of 50% from baseline to posttreatment was significantly more often seen in participants of the intervention group (QIDS: 37/102 = 36.3%; HRSD: 34/102 = 33.3%) as compared to the control group (QIDS: 22/102 = 21.6%; $\chi^2(1, n = 204) = 5.365$, $p = 0.015$; HRSD: 19/102 = 18.6%; $\chi^2(1, n = 204) = 5.735$, $p = 0.012$). This resulted in a NNT of 7 for both QIDS (95% CI 3.7–41.2) and the HRSD (95% CI 3.8–35.2), respectively, to achieve one additional treatment response as compared to the control group. A reliable change from baseline to posttreatment in depressive symptom severity was seen significantly more often in the intervention group (QIDS: 46/102, 45.1%; HRSD: 41/102, 40.2%) compared with the control condition (QIDS: 29/102, 28.4%; $\chi^2(1, n = 204) = 6.09$, $p = .001$; HRSD: 22/102, 21.6%; $\chi^2(1, n = 204) = 8.29$, p = .004). This resulted in an NNT of 7 (95% CI 3.4–27.5) based on the QIDS and 6 (95% CI 3.2–16.1) based on the HRSD to achieve one additional treatment response compared to the control group. Seeing a reliable improvement was one and a half times to almost twice as likely in the intervention group compared to the control condition (QIDS: likelihood ratio = 1.59, 95% CI 1.09–2.31; HRSD: likelihood ratio = 1.86, 95% CI 1.20–2.89). There were higher rates of symptom deterioration from baseline to posttreatment in the control group when

Table 2
Means, SD and Effect Sizes (95% CIs) for the Clinical Outcomes Based on the Imputed Data Set (*N*=204)

| | Pre-assessment | | Post-assessment | | 3-month FU | | Between-group effect size Cohen's d (95% CI) | |
|---|---|---|---|---|---|---|---|---|
| | Mean | *SD* | Mean | *SD* | Mean | *SD* | pre-post | pre-3-month FU |
| QIDS-C | | | | | | | 0.37 (0.09-0.64) | |
| INT | 8.18 | 3.62 | 4.98 | 3.11 | | | | |
| CTR | 8.11 | 3.89 | 6.25 | 3.22 | | | | |
| HRSD | | | | | | | 0.23 (-0.05-0.50) | |
| INT | 13.72 | 6.21 | 9.60 | 5.60 | | | | |
| CTR | 14.62 | 6.81 | 11.59 | 5.86 | | | | |
| CES-D | | | | | | | 0.71 (0.43-0.99) | 0.66 (0.38-0.95) |
| INT | 26.67 | 6.50 | 17.79 | 7.03 | 17.32 | 8.33 | | |
| CTR | 27.73 | 7.50 | 24.06 | 7.85 | 24.29 | 8.90 | | |
| AQoL total score | | | | | | | | |
| INT | 61.66 | 7.81 | 67.53 | 7.57 | 69.09 | 8.58 | 0.68 (0.39-0.96) | 0.68 (0.40-0.96) |
| CTR | 61.03 | 9.87 | 62.43 | 9.81 | 62.99 | 10.55 | | |
| AQoL MCS | | | | | | | 0.65 (0.37-0.94) | 0.74 (0.45-1.02) |
| INT | 62.18 | 7.68 | 67.27 | 7.40 | 69.18 | 8.47 | | |
| CTR | 61.91 | 10.01 | 62.80 | 9.70 | 63.23 | 9.90 | | |
| AQoL PCS | | | | | | | 0.55 (0.27-0.83) | 0.46 (0.18-0.74) |
| INT | 60.40 | 9.65 | 68.17 | 9.30 | 68.86 | 9.96 | | |
| CTR | 58.90 | 11.04 | 61.52 | 11.55 | 62.37 | 13.26 | | |
| HADS-A | | | | | | | 0.41 (0.13-0.68) | 0.63 (0.35-0.92) |
| INT | 9.63 | 3.14 | 8.10 | 2.98 | 7.23 | 3.20 | | |
| CTR | 9.38 | 3.20 | 8.78 | 3.20 | 8.72 | 3.52 | | |
| BADS-SF | | | | | | | 0.63 (0.35-0.91) | 0.45 (0.17-0.83) |
| INT | 25.70 | 7.89 | 32.37 | 7.34 | 31.87 | 7.65 | | |
| CTR | 26.80 | 6.69 | 28.65 | 7.75 | 29.43 | 8.31 | | |
| SPSI-NPO | | | | | | | 0.05 (-0.23-0.32) | 0.10 (-0.23-0.32) |
| INT | 7.26 | 4.54 | 6.54 | 4.30 | 5.92 | 3.93 | | |
| CTR | 6.83 | 4.82 | 5.87 | 4.44 | 5.69 | 4.13 | | |
| SPSI-PPO | | | | | | | 0.44 (0.16-0.72) | 0.29 (0.01-0.56) |
| INT | 9.45 | 3.94 | 10.69 | 3.54 | 10.68 | 3.44 | | |
| CTR | 9.71 | 3.71 | 9.83 | 3.62 | 10.02 | 4.04 | | |
| PSWQ | | | | | | | 0.43 (0.15-0.71) | 0.53 (0.25-0.81) |
| INT | 9.78 | 3.92 | 6.98 | 3.49 | 7.00 | 3.83 | | |
| CTR | 9.77 | 4.04 | 8.75 | 4.32 | 9.15 | 4.51 | | |
| ISI | | | | | | | 0.41 (0.14-0.69) | 0.54 (0.26-0-82) |
| INT | 12.73 | 5.46 | 10.11 | 5.41 | 9.40 | 5.36 | | |
| CTR | 11.92 | 6.02 | 11.36 | 5.89 | 11.29 | 6.18 | | |
| PSMS | | | | | | | 0.18 (-0.18-0.45) | 0.52 (0.24-0.80) |
| INT | 18.71 | 3.36 | 19.54 | 3.21 | 20.44 | 3.46 | | |
| CTR | 19.06 | 3.15 | 19.41 | 3.38 | 19.36 | 3.67 | | |
| AUDIT | | | | | | | 0.23 (-0.04-0.51) | 0.25 (-0.03-0.53) |
| INT | 4.39 | 4.28 | 3.68 | 3.73 | 3.57 | 3.60 | | |
| CTR | 4.34 | 4.43 | 3.97 | 4.53 | 4.00 | 4.66 | | |

*Note.* SD = Standard deviation. CI = confidence interval. FU = follow-up. INT = intervention group (n=102). CTR = control group (n=102). HRSD = Hamilton Rating Scale for Depression. QIDS-C = Quick Inventory of Depressive Symptomatology – Clinician rating. CES-D = Center for Epidemiological Depression Scale. AQoL = Assessment of Quality of Life. HADS – A = Hospital Anxiety and Depression Scale. BADS-SF = Behavioural Activation for Depression Scale Short Form. SPSI – NPO = Social Problem-Solving Inventory - negative problem orientation. SPSI – PPO = Social Problem-Solving Inventory - positive problem orientation. PSWQ = Penn State Worrying Questionnaire (ultra brief version). ISI = insomnia Severity Index. PSMS = Pearlin Mastery Scale. AUDIT = Alcohol Use Disorders Identification Test.

compared to the intervention group, but this did not reach statistical significance (QIDS: intervention group: 3/102, 2.9%; control group: 5/102, 4.9%; $\chi^2$ (1, $n$ = 204) = 0.52, $p$ = .36; HRSD: intervention group: 5/102, 4.9%; control group: 12/102, 11.8%; $\chi^2$ (1, $n$ = 204) = 3.14, $p$ = .06). Based on the QIDS and the HRSD, significantly more participants in the intervention group met the criteria for symptom-free status (QIDS: 46/78, 59% vs. 26/73, 35.6%; $\chi^2$ (1, $n$ = 151) = 8.247,

$p$ = 0.003; HRSD: 31/72, 43.1% vs. 22/78, 28.2%; $\chi^2$ (1, $n$ = 150) = 3.614, $p$ = 0.042). The corresponding NNT was 5 for the QIDS (95% CI 2.6-12.7) and 7 for the HRSD (95% CI -3–22.7), respectively.

*Longer-Term Effects*

There were no changes in depression symptom severity from posttreatment to follow-up, neither in the intervention group, $t(101) = -.654$, $p = .51$, nor in the control group, $t(101) = .100$, $p = .92$, indicating that initially achieved changes from baseline to posttreatment were sustained over time. ANCOVAs controlling for baseline depression severity showed a statistically significant between-group difference in CES-D scores at follow-up favoring the intervention group, F(1, 201) = 34.80, $p < .001$. This difference corresponded to an effect size of 0.66 (95% CI 0.38–0.95). Between-group differences for secondary outcomes were still significant at the 3-month follow-up except for negative problem-orientation (subscale of the SPSI; $p = .82$) and alcohol use disorders (AUDIT; $p = .12$).

*Sensitivity Analyses*

More participants in the control group (6/102, 5.9%) received treatment during the follow-up period compared to the intervention group (4/102, 3.9%). However, this difference was not statistically significant, $\chi^2$ (1, $n$ = 204) = 0.421, $p = .52$. Neither treatment duration (posttreatment: $F[1, 99] = .162$, $p = .69$; 3-month follow-up: $F[1, 99] = .341$, $p = .56$) nor receiving treatment during the follow-up period (posttreatment $F[1, 200] = .302$, $p = .58$; 3-month follow-up: $F[1, 200] = .013$, $p = .91$) were significant predictors of the outcome. Sensitivity analyses based on the study completers' sample did not result in a different interpretation of the primary intervention outcome, $F(1, 166) = 14.59$, $p > .001$.

## Discussion

Findings of the present study support the primary hypothesis that the intervention resulted, compared to a nontreated control group, in lower depressive symptom severity in participants with subthreshold depression. This finding was replicated both in self-reported and in two observer-based ratings of depressive symptom severity. Effects were also found for a number of relevant secondary outcomes such as health-related quality of life, worrying, behavioral activation, anxiety, and sleep problems. No effects were found for mastery, negative problem orientation, and comorbid problematic alcohol use.

The effects observed in the present study are in line with findings of another recent meta-analysis on psychological interventions for subthreshold depression (Cuijpers, Koole, et al., 2014). Moreover, the current study extends these findings by showing that a psychological intervention can have clinically relevant effects on observer-rated depressive symptom severity. Effect sizes on most assessed outcomes were above the suggested cutoff of a minimal important difference of a standardized mean difference of 0.24 in the treatment of depression (Cuijpers, Turner, et al., 2014). The number-needed-to-treat (NNT) ranged from between 5 and 7 to achieve one additional treatment response or symptom-free status, and depended on the outcome measure used. Similar numbers are found for antidepressants in the treatment of major depression (Guirguis-Blake, 2010). All in all, the observed effects can be interpreted as clinically relevant. However, little is known about the actual impact these effects have on patients' lives. In addition, using the same approach applied to characterize clinically significant change in major depression may not be valid in subthreshold depression. It is worth noting that the effect sizes for most secondary outcomes were similar to those found in the first RCT evaluating this novel web-based intervention (Buntrock et al., 2015; Buntrock et al., 2016). While in the first RCT the intervention was delivered with substantial human support from a psychologist (approximately 3 hours per participant), the present study found clinically meaningful effects without providing individual written feedback on each session. The observed difference between self-report and observer-based depressive symptom severity is in line with previous research (Cuijpers, Koole, et al., 2014). However, a meta-analysis on self-reported versus clinician-rated symptoms of depression showed a higher effect size for clinician-rated instruments as compared to self-report instruments (Cuijpers, Li, Hofmann, & Andersson, 2010). Depending on the symptom severity of an individual, self-report or clinician ratings might be more suitable. Therefore, it seems best to include both kinds of assessment in clinical research.

Other key findings of our study can be summarized as follows. First, effects on self-reported depression severity were large in size, which further supports the potential benefits of treating depressive symptoms at a very early disease stage. Studies on the prevention of depression indicate that the treatment of subthreshold depression may not only reduce symptom severity, but may also help to prevent further deterioration of symptoms and prevent the onset of a full-blown major depression (Buntrock et al., 2016; van Zoonen et al., 2014). Second, our study shows that clinically important results can be achieved in a less intensive guidance

format. Instead of providing detailed feedback after each completed session, the e-coach simply monitored the adherence to the intervention and only provided feedback on the content on request of participants. Surprisingly few participants asked for content feedback: 15 in 102 participants, averaging at 0.15 feedbacks per participant. The e-coaches spent on average 30 minutes on each participant, and most of the resources spent for coaching were utilized to monitor the adherence to the intervention. Hence, the question arises whether or not automated reminders, in combination with feedback on demand, have a similar effect while requiring even fewer resources. Although 3 hours of psychological support per participant is already much less than in individual face-to-face CBT interventions, even more patients with subthreshold depression could be treated for the same costs if meaningful results are achieved using less therapists' time. Third, noncompleters did not differ from intervention completers regarding QIDS scores at posttreatment. This might be an indication that intervention dropout might not necessarily be related to treatment success. Participants might not proceed with the intervention because they already achieved sufficient improvements. However, more research is needed to support such an assumption and to explore the relationship between treatment dropout and success in web-based interventions for (subthreshold) depression. Fourth, the large effects found in the present study are in line with the assumption that higher effect sizes frequently found for guided vs. unguided self-help interventions (Baumeister, Reichler, Munzinger, & Lin, 2014) are attributable to the adherence-promoting factor of human support. This has also been stated previously in the supportive accountability model of human support in Web-based intervention (Mohr et al., 2011). However, randomized controlled trials that compare adherence-focused guidance format with regular content feedbacks are needed to support such an assumption and to determine whether or not adherence-focused guidance formats result in outcomes equivalent to those of more intensive content-focused guidance formats. Even if a less intensive guidance format should yield lower effects in direct comparisons, their potential on a population level might still be higher, as such interventions can be distributed to more participants for a given budget of health care resources. On the other hand, it may very well be the case that patients with subthreshold depression are less willing to participate in interventions in which no regular content-feedback from a health care provider is offered, which would result in a lower reach and thus lower overall effects in the target population. Thus, future studies should compare the acceptability, effectiveness, cost-effectiveness, and reach of different guidance formats for subthreshold depression.

This study has the following limitations. First, we cannot rule out a potential selection bias while recruiting participants. Moreover, participants in our study were predominantly female. Hence, conclusions from the present study may not generally apply, for example, to population segments recruited by different recruitment strategies (i.e., patients recruited in primary or secondary mental health care). However, this is a common finding in web-based intervention trials (Andersson & Titov, 2014), indicating that results may generally apply to a population that is interested in web-based interventions. Future studies that apply different recruitment strategies for the evaluation of web-based interventions for subthreshold depression (i.e., with referral from general practitioners) are needed. Second, participants were not blind to the study group they were allocated to. Third, the lack of long-term follow-up and assessment of progression to a full-blown major depressive disorder is a limitation to the study. Future studies should include a longer-term follow-up to assess the preventive effects of web-based interventions with adherence-focused guidance. Fourth, we also did not assess whether participants fulfilled criteria for an anxiety disorder at baseline. Patients with comorbid anxiety disorder might benefit to a different extent from the intervention compared to those without, which should be investigated in future studies. Fifth, the study may have benefited from an inclusion of physiological measures. Future studies could consider complementing self-reports and observer-based instruments with objective measurements (such as inflammatory markers). Sixth, we did not monitor changes in medication during the trial period; hence, we cannot rule out that this might have biased the results. Seventh, although the current study replicated the results of the first RCT on this newly developed intervention, future studies are needed to reliably estimate the potential effects of web-based interventions for subthreshold depression in different target populations (e.g., in individuals with comorbid chronic conditions or problematic substance use; Schaub et al., 2016). Eighth, although patients in the control group had full access to treatment as usual, we cannot rule out a potential nocebo effect in the control condition (Furukawa et al., 2014). Finally, although the majority of the participants reached a symptom-free status during the trial, a substantial number of participants did not. Hence, future studies should investigate whether these participants would profit from other forms of treatments, such as face-to-face

psychotherapy or antidepressant medication, and whether it is possible to identify these individuals on an individual level on the basis of a multivariate set of baseline predictors (Kessler, van Loo, Wardenaar, Bossarte, Brenner, Cai, et al., 2016; Kessler, van Loo, Wardenaar, Bossarte, Brenner, Ebert, et al., 2016). The use of scalable web-based interventions based on recent advancements, such as advantages in machine-learning techniques, may help to obtain large enough sample sizes that are necessary to overcome the statistical power problem in the development of such prediction algorithms.

In conclusion, the present study adds to the growing evidence base that psychological interventions can result in substantial benefits for individuals with subthreshold depressive symptoms. Moreover, the present study further adds to the growing evidence base that web-based guided self-help has a high potential for delivering effective low-threshold mental health interventions. Results of the present study also indicate that web-based interventions for subthreshold depression can be delivered with limited human support without a substantial loss of effects, thus potentially reaching a much greater population at the same cost as interventions with more intensive human support.

### Conflict of Interest Statement

The authors declare that there are no conflicts of interest.

## Appendix A. Supplementary Data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.beth.2017.05.004.

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